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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,098	10/14/2004	Akira Ideno	Q83564	9139

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,098	IDENO ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-36,38,39 and 41-64* is/are pending in the application.

4a) Of the above claim(s) *38,39,43-52,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36,41,42,53-56 and 60-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *complete copy of Iida cited on IDS of 12/08*.

In a telephone interview with Janice Lee on 3/25/09 applicants agreed to amend the claims of the instant case so as to overcome all previous rejections of record. The amendments agreed to included amending part (b) of claim 33 to add "to encode a fusion protein between the PPIase and the desired protein" at the end and to add "comprising an IF domain" at the end of the final wherein clause of the claim as well as some minor cosmetic changes to claims 42, 60, 61 and 64 and cancellation of non-elected claims. However, following this agreement new art was discovered which reads on the claimed invention as well as the claims as they would have been amended. The after-final amendment submitted on 2/20/09 will be entered and the finality of the previous Office Action is hereby withdrawn and new grounds of rejection are presented below.

Claims 1-32, 37, and 40 have been canceled. Claims 33-36, 38, 39, and 41-64 are still at issue and are present for examination. Claims 38, 39, 43-52 and 57-58 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 5/23/07.

Applicants' arguments filed on 2/20/09, have been fully considered and are deemed to be persuasive to overcome some of

the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Fersht (WO 00/75346) in view of Furutani et al. is withdrawn as applicants have presented sufficient evidence to conclude that the showing of unexpected results for the TcFKfusion2 vector comprising the *Thermococcus* sp. KS-1 short type FKBP-type PPIase (TCFKBP18) coding sequence presented in the 1.132 declaration of 11/09/2007 would be representative of the results for vectors comprising a coding region for other archaebacterial FKBP-type PPIases. Applicants have provided sufficient information to conclude that the IF domain of archaebacterial FKBP-type PPIases is critical for chaperone function of these PPIases, that other proteins with chaperone function but lacking any IF domain such a that of Fersht do not show the same results and that at least two other vectors comprising different archaebacterial FKBP-type PPIases comprising an IF domain also exhibit the same results.

Claims 60 and 61 are objected to because of the following informalities: the recitation of "to produce the fused protein in a cytoplasm of said host cell" in claim 60 and "to produce the fused protein in a periplasm or a medium of said host cell"

in claim 61 implies that a host cell includes more than one cytoplasm, periplasm or medium but this is not the case. It is suggested that the indefinite article "a" preceding each of cytoplasm, periplasm, and medium in these claims be replaced with the definite article "the". Appropriate correction is required.

Claims 35 and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is confusing as to whether the claim requires a sequence encoding a protease digestion site to actually be present in the claimed vector or if the vector only requires that a protease digestion site can be inserted therein. It is noted that if the claim does not in fact require the presence of a sequence encoding the protease digestion site that the claim is not further limiting of claim 33 as the junction between any two nucleotides of any vector is a site at which something else can be inserted. Claim 35 is further confusing in the recitation of "a second coding region" as claim 33 from which this claim depends already recites a different "second coding region". It is suggested that claim 35 be amended to replace "in which a second coding region can be inserted, wherein the

region" with "in which a third coding region is inserted, wherein the third coding region". For further examination claim 35 is interpreted as requiring the presence of a sequence encoding a protease digestion site.

The structure of claim 64 is such that it makes it unclear if the process of claim 59 is an active step of the process of claim 64 or not. It is suggested that claim 64 be amended to recite "A process for producing a desired protein, which comprises producing a fused protein by the process of claim 59 and digesting the fused protein with a protease that digests the protease digestion site.".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33, 35, 36, 42, 55, 56, 59, 60 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Iida et al. (Reference 1 of Applicants IDS of 12/1/09, note a second copy of this reference is attached to this office action as the copy submitted by applicants is missing all even numbered pages of the reference).

Iida et al. teach a vector encoding a fusion protein comprising an archaebacterial FKBP-type PPIase from *Halobacterium cutirubrum* fused to glutathione S-transferase (GST) at a *Bam*HI restriction site (pGEX-HcFK-1, see page 320). The fusion protein comprises a protease cleavage site between the coding regions of GST and the FKBP PPIase. The archaebacterial FKBP-type PPIase from *Halobacterium cutirubrum* comprises an IF domain and suppressed aggregation of unfolded rhodanese and thus has molecular chaperone activity. Iida et al. further teach transformation of this vector into *E. coli* and the expression of the fusion protein in the cytoplasm of said *E.coli* followed by cleavage of the fusion protein with a protease which cleaves at the protease digestion site. As such Iida et al. anticipate all of the instant claims

Claims 33, 41, 42, 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Furutani et al. (see IDS of 7/23/08).

Furutani et al. teach an expression vector (pTFK, see page 455) encoding an archaebacterial FKBP-type PPIase from *Methanococcus thermolithotrophicus* and having a *Bam*HI restriction site following the FKBP-type PPIase coding sequence. Furutani et al. further teach transformation of this vector into *E. coli*. The archaebacterial FKBP-type PPIase from

Methanococcus thermolithotrophicus is a short-type FKBP-type PPIase, has moleculare chaperone activity and comprises an IF domain.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 53, 54, 61, 62, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scholz et al. (US PG-PUB 2003/0096352) in view of Iida et al. (Reference 1 of Applicants IDS of 12/1/09).

Scholz et al. teach expression vectors for producing a fusion protein comprising a chaperone polypeptide which is a PPIase fused in frame to a protein of interest. Preferably the chaperone polypeptide is *E. coli* FkpA, SlyD or trigger factor which are FKBP-type PPIases. (see paragraphs 13, 14, 32, 41, and

42). Scholz et al teaches that suitable proteins of interest include antibodies and membrane proteins (see paragraph 38). Scholz et al. further teach the inclusion of a suitable restriction site for insertion of the sequence encoding the protein of interest following the chaperone polypeptide (see paragraph 50), sequences encoding a protease digestion site between the chaperone polypeptide and the protein of interest (see paragraph 50 and 64) and inclusion of a signal sequence preceding the chaperone polypeptide encoding region for the secretion of the fusion protein (see paragraph 38). Scholz et al. further teach that the expression vectors may be used to express the fusion protein in a cell-free translation system (see paragraph 66). Scholz et al. do not specifically teach the use of an archaebacterial FKBP-type PPIase.

Iida et al. teach an archaebacterial FKBP-type PPIase from *Halobacterium cutirubrum* which comprises an IF domain and suppressed aggregation of unfolded rhodanese and thus has molecular chaperone activity.

Therefore, as the protein disclosed by Iida et al. has all the properties of the first region of the fusion vectors of Scholz et al. (i.e. FKBP type PPIase activity and molecular chaperone activity), it would have been obvious to one of ordinary skill in the art to select the PPIase of *Halobacterium*

cutirubrum for use in the fusion vectors of Scholz et al. Furthermore, as all FKBP-type PPIases bind the immunosuppressant FK-506, it would have been obvious to one of ordinary skill in the art to use this immunosuppressant bound to a carrier as a suitable affinity ligand for isolating the expressed fusion proteins.

Claims 34-36, 53, 54, and 60-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scholz et al. (US PG-PUB 2003/0096352) in view of Furutani et al. (see IDS of 7/23/08).

Scholz et al. teach expression vectors for producing a fusion protein comprising a chaperone polypeptide which is a PPIase fused in frame to a protein of interest. Preferably the chaperone polypeptide is *E. coli* FkpA, SlyD or trigger factor which are FKBP-type PPIases. (see paragraphs 13, 14, 32, 41, and 42). Scholz et al teaches that suitable proteins of interest include antibodies and membrane proteins (see paragraph 38). Scholz et al. further teach the inclusion of a suitable restriction site for insertion of the sequence encoding the protein of interest following the chaperone polypeptide (see paragraph 50), sequences encoding a protease digestion site between the chaperone polypeptide and the protein of interest (see paragraph 50 and 64) and inclusion of a signal sequence

preceding the chaperone polypeptide encoding region for the secretion of the fusion protein (see paragraph 38). Scholz et al. further teach that the expression vectors may be used to express the fusion protein in a cell-free translation system (see paragraph 66). Scholz et al. do not specifically teach the use of an archaebacterial FKBP-type PPIase.

Furutani et al. teach an archaebacterial FKBP-type PPIase from *Methanococcus thermolithotrophicus*. The archaebacterial FKBP-type PPIase from *Methanococcus thermolithotrophicus* is a short-type FKBP-type PPIase, has molecular chaperone activity and comprises an IF domain.

Therefore, as the protein disclosed by Furutani et al. has all the properties of the first region of the fusion vectors of Scholz et al. (i.e. FKBP type PPIase activity and molecular chaperone activity), it would have been obvious to one of ordinary skill in the art to select the PPIase of *Methanococcus thermolithotrophicus* for use in the fusion vectors of Scholz et al. Furthermore, as all FKBP-type PPIases bind the immunosuppressant FK-506, it would have been obvious to one of ordinary skill in the art to use this immunosuppressant bound to a carrier as a suitable affinity ligand for isolating the expressed fusion proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652